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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte STEPHEN QUIRK and DAVID JOHN TYRRELL

Appeal 2009-013418
Application 10/026,393
Technology Center 1600

Decided: April 5, 2010

Before DONALD E. ADAMS, LORA M. GREEN, and
JEFFREY N. FREDMAN, *Administrative Patent Judges.*

FREDMAN, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to methods of detecting metalloproteinases in a chronic wound. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

Statement of the Case

Background

"Chronic wounds that do not heal well are characterized by an increase in the activity of proteinase enzymes including, but not limited to, matrix metalloproteinases (MMPs)" (Spec. 2, ll. 1-3). According to the Specification "[s]ince the level of these enzymes is constantly in flux within a chronic wound, it is therapeutically important to specifically identify which proteinase, whether an enzyme or proenzyme, is at high levels" (Spec. 2, ll. 32-34).

The Claims

Claims 82-96 are on appeal. Claims 82 and 90 are representative and read as follows:

> 82. A method for simultaneously detecting the presence of at least two different metalloproteinases in a chronic wound of a human or an animal, the method comprising:
>
> a) collecting a sample of fluid from the chronic wound, the sample comprising at least two different metalloproteinases;
>
> b) exposing the sample to a plurality of target antibodies, wherein a first target antibody is configured to bind with a first metalloproteinase to form a first target antibody/metalloproteinase complex, and a second target antibody is configured to bind with a second metalloproteinase to form a second target antibody/metalloproteinase complex; and
>
> c) simultaneously identifying the first metalloproteinase and the second metalloproteinase by determining the presence or absence of a detectable or measurable manifestation of a first signal element bound to the first target antibody and a second signal element bound to the second target antibody.

90. The method of claim 82, wherein the first signal element and the second signal element are the same.

The prior art

The prior art relied upon by the Examiner is found at pages 2-4 of the Examiner's Answer.

The issues

A. The Examiner rejected claims 82-96 under 35 U.S.C. § 103(a) as being obvious over Sorsa, Rowe, and Sodek (Ans. 4-6).

B. The Examiner rejected claim 90 under 35 U.S.C. § 112, first paragraph as not being enabled for identifying two or more metalloproteinases in a mixed sample using a single signal element wherein the metalloproteinases are not initially separated (Ans. 6-8).

C. The Examiner rejected claim 90 under 35 U.S.C. § 112, first paragraph as not describing a method for identifying two or more metalloproteinases in a mixed sample using a single signal element wherein the metalloproteinases are not initially separated (Ans. 6-8).

A. 35 U.S.C. § 103(a) over Sorsa, Rowe, and Sodek

The Examiner concludes that it would have been obvious to the ordinary artisan to "incorporate the array approach of Rowe et al into the methods of Sorsa et al. In such a combined method, a sample of gingival crevicular fluid from a patient with periodontal disease, comprising a plurality of metalloproteases, would be reacted with particle-bound labeled antibodies specific for each protease" (Ans. 6). The Examiner concludes that "[m]otivation to thus combine the methods of Sorsa et al and Rowe et al

is derived from the fact that metalloproteases, including MMP-8 and MMP-9, are involved in periodontal disease" (Ans. 6)

Appellants argue that the prior art does not teach detection of MMPs in chronic wounds, specifically that "whether considering the accepted clinical definition of a chronic wound, as mentioned above, or combining the standard definition of 'chronic' with that of 'wound', a periodontitis lesion, as defined and used by Sorsa, et al., is not synonymous with the term 'chronic wound'" (App. Br. 14).

Appellants argue that "it is respectfully submitted that no proper motivation exists to combine the teachings of Sorsa, et al. with those of Rowe, et al. and any such modification of the cited references relies on the impermissible use of hindsight" (App. Br. 7). Appellants argue that "[n]either Rowe, et al. nor Sodek, et al. provide a motivation for ignoring the aspects of Sorsa, et al. that teach a method for detecting periodontal disease through detection of only MMP-8, and the exclusion of other MMPs" (App. Br. 10).

In view of these conflicting positions, we frame the obviousness issue before us as follows:

Does the evidence of record support the Examiner's conclusion that one of skill in the art would have been motivated to combine the cited references, and that doing so would lead a skilled worker to a method meeting the limitations of claim 82?

Findings of Fact

1. The Specification does not define the term "chronic wounds" but teaches that "[o]pen cutaneous wounds represent one major category of

chronic wounds, which also include burn wounds, neuropathic ulcers, pressure sores, venous stasis ulcers, and diabetic ulcers" (Spec. 1, ll. 17-19).

2. Sorsa teaches that:

> Periodontal disease comprises a group of inflammatory disorders originating from infections affecting the gingiva (gum) and the alveolar (jaw) bone structures supporting the teeth. The primary cause of periodontal diseases is bacterial plaque attached to the teeth. This causes inflammation of the gum which may result in destruction of the actual tooth-supporting structure and bone. In periodontal disease, there is usually a large accumulation of bacteria in plaque, both above (supragingival) and below (subgingival) the gum line. The plaque can calcify and form calculus deposits. The calculus deposit and associated plaque can create a "pocket" between the teeth and the gingiva which is characteristic of the periodontal disease.

(Sorsa, col. 1, ll. 21-34).

3. Sorsa teaches that the prior art found "elevated collagenase activity (MMP-1 and MMP-8) and gelatinases (MMP-2 and MMP-9) in extracts of inflamed gingival tissues, gingival crevicular fluid and salivary/mouthrinse-samples of periodontitis patients (Sorsa, T., et al., Ann. N.Y. Acad. Sci., 732: 112-131, 1994)" (Sorsa, col. 6, ll. 2-7).

4. Sorsa teaches that the "activities of these proteinases have been found to be positively correlated with the severity of periodontal inflammation and pocket depth at the periodontitis lesion sites donating these proteinases to gingival extracellular matrix and adjacent gingiva" (Sorsa, col. 6, ll. 8-12).

5. Sorsa teaches that "a method specific for MMP-8 in periodontitis gingival crevicular fluid would be optimal in addressing the course of tissue destruction events in periodontitis" (Sorsa, col. 8, ll. 1-3).

6. Sorsa teaches that "[g]ingival crevicular fluid sample is collected with a sampling device. . . . The sample is then contacted with at least one monoclonal antibody, which is already attached to the sampling or test device or can be added to the combined sampling and test device" (Sorsa, col. 15, ll. 39-46).

7. Sorsa teaches that "[w]estern blot analysis using both anti-human MMP-8 and anti-human MMP-1 from the sample material given in Table 1 show that MMP-8 existed in 70-75 kD inactive or latent and 65 kD active forms, and MMP-1 was not detected" (Sorsa, col. 17, ll. 45-48).

8. Sorsa teaches that in making antibodies to proMM-8 for use in the assay, the "clones are also tested for their cross-reaction to enzymes structurally and immunologically related to MMP-8 which may be present in gingival crevicular fluid samples (e.g., PMN-gelatinase [MMP-9], fibroblast type collagenase [MMP-1] and stromelysin-1 [MMP-3])" (Sorsa, col. 20, l. 64 to col. 21, l. 2).

9. Rowe teaches the "array biosensor is designed to test multiple samples for the presence of any of several analytes" (Rowe 3846, col. 2).

10. Rowe teaches that the "array biosensor demonstrated the capability of performing simultaneous assays for very different types of analytes on a single substrate" (Rowe 3851, col. 2).

11. Rowe teaches that the "array biosensor utilizes evanescent wave excitation to interrogate patterns of fluoroimmunoassays immobilized on the planar waveguide. This system detects and measures analytes in buffer and

in a number of physiological fluids and is relatively unaffected by nonspecifically bound components from complex samples" (Rowe 3847, col. 1).

12. Sodek teaches that in "patients with either adult periodontitis or with localized juvenile periodontitis the levels of active collagenase were >15-fold higher than in control groups where active collagenase levels were generally low. However, total collagenase was not significantly different between the groups because of the presence of latent collagenase in control group samples" (Sodek 355, col. 1).

13. Sodek teaches that "[a]nalysis of gelatinase activity also showed significantly higher levels of the enzyme in the periodontitis groups" (Sodek 355, col. 1).

Principles of Law

The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) secondary considerations of nonobviousness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). The Supreme Court has emphasized that "the [obviousness] analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR Int'l v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). As noted by the Court in *KSR*, "[a] person of ordinary skill is also a person of ordinary creativity, not an automaton." 550 U.S. at 421.

Claim terms are interpreted using the broadest reasonable interpretation in light of the Specification. *See, e.g., In re Hyatt*, 211 F.3d 1367, 1372 (Fed. Cir. 2000) ("[D]uring examination proceedings, claims are given their broadest reasonable interpretation consistent with the specification."). *Also see In re Morris*, 127 F.3d 1048, 1054-56 (Fed. Cir. 1997). ("Absent an express definition in their specification, the fact that appellants can point to definitions or usages that conform to their interpretation does not make the PTO's definition unreasonable when the PTO can point to other sources that support its interpretation.")

Analysis

Claim Interpretation

Claim interpretation is at the heart of patent examination because before a claim is properly interpreted, its scope can not be compared to the prior art. In this case, Appellants challenge the Examiner's interpretation of the phrase "chronic wound" as recited in Claim 82, arguing that "whether considering the accepted clinical definition of a chronic wound, as mentioned above, or combining the standard definition of 'chronic' with that of 'wound', a periodontitis lesion, as defined and used by Sorsa, et al., is not synonymous with the term 'chronic wound'" (App. Br. 14). Appellants argue that a periodontitis pocket "is not an injury or damage caused by physical means persisting over a long period of time, it is not an injury in which the skin or other external organic surface is torn, pierced, cut or otherwise broken . . . and it is not produced by trauma or pathologic insult" (App. Br. 14).

During prosecution, claim terms are given their broadest reasonable interpretation as they would be understood by persons of ordinary skill in the

art in the light of the Specification. Therefore, we first turn to the Specification to determine whether the meaning of the phrase "chronic wound" can be discerned.

The Specification teaches that "[o]pen cutaneous wounds represent one major category of chronic wounds, which also include burn wounds, neuropathic ulcers, pressure sores, venous stasis ulcers, and diabetic ulcers" (Spec. 1, ll. 17-19; FF 1).

Appellants do not identify any portion of the Specification which specifically defines the term "chronic wound", but instead relies upon dictionary definitions of the terms "chronic" and "wound" (*see* App. Br. 13-14).

The Examiner finds that "the skilled artisan would, more likely than not, interpret periodontitis as involving chronic wounds" (Ans. 18).

We find that the Examiner has the better position here. There is no dispute that periodontal disease may be "chronic", only that it is not a type of "wound." Appellants' Specification contradicts Appellants' argument to limit wounds to injuries caused by physical means or to breaking or tearing of skin or external surfaces (*see* App. Br. 14). The Specification expressly recognizes that "diabetic ulcers" are a type of chronic wound, and diabetic ulcers are not necessarily caused by physical means or tearing of the skin (FF 1).

Therefore, we find that the term "chronic wound" in Claim 82 reasonably encompasses the periodontitis of Sorsa and Sodek, a chronic condition which results in "inflammation of the gum which may result in destruction of the actual tooth-supporting structure and bone" (Sorsa, col. 1, ll. 25-27; FF 2).

Obviousness

Sorsa teaches a method in which MMPs in crevicular fluid from the periodontitis patient is collected and assayed for matrix metalloproteinases using antibody binding (FF 3-6). Sorsa expressly teaches attempts at detection of two different MMPs, MMP-1 and MMP-8, by Western blotting, an antibody based detection technique (FF 7). Sorsa teaches that other MMPs may be present in gingival crevicular samples including MMP-8, MMP-9, MMP-1, and MMP-3 (FF 8).

Rowe is simply relied upon to demonstrate that the state of the art permits the use of protein arrays for detection of proteins of interest with antibody assays (FF 9-11).

Sodek is relied upon to further evidence that multiple MMPs are found in gingival crevicular samples and are of interest in periodontitis (FF 12-13).

Appellants argue that "it is respectfully submitted that no proper motivation exists to combine the teachings of Sorsa, et al. with those of Rowe, et al. and any such modification of the cited references relies on the impermissible use of hindsight" (App. Br. 7).

We are not persuaded. While we are fully aware that hindsight bias often plagues determinations of obviousness, *Graham v. John Deere Co.*, 383 U.S. 1, 36 (1966), we are also mindful that the Supreme Court has clearly stated that the "combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results," *KSR*, 550 U.S. at 401.

This reasoning is applicable here. We find that applying the method of Sorsa to detect all of the MMPs suspected of being present in gingival

crevicular samples as taught by Sorsa and Sodek would have yielded the predictable result of a more "efficient determination of which proteases are present in patient samples for research analysis and/or clinical treatment" (Ans. 6).

Appellants argue that "[n]either Rowe, et al. nor Sodek, et al. provide a motivation for ignoring the aspects of Sorsa, et al. that teach a method for detecting periodontal disease through detection of only MMP-8, and the exclusion of other MMPs" (App. Br. 10).

We are not persuaded. Sorsa, while focused on the detection of MMP-8 (FF 5), teaches that other MMPs may be found in periodontitis (FF 8). Further, Sodek clearly teaches that multiple MMPs are found in periodontitis (FF 12-13). Like our appellate reviewing court, "[w]e will not read into a reference a teaching away from a process where no such language exists." *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1364 (Fed.Cir. 2006).

Appellants argue that "none of the cited references disclose or suggest the step of 'collecting a sample from the fluid of a chronic wound', and then simultaneously identifying at least two different metalloproteinases in such a fluid" (App. Br. 12).

We are not persuaded. First, as we have already noted, Sorsa performs a Western blot on crevicular fluid from periodontitis patients which simultaneously detected the presence or absence of MMP-1 and MMP-8 (FF 7). Further, the entire reason that Rowe is present in the rejection is to demonstrate that the ordinary artisan can routinely apply protein arrays for the simultaneous detection of multiple proteins of interest (FF 9-11).

Conclusion of Law

The evidence of record supports the Examiner's conclusion that one of skill in the art would have been motivated to combine the cited references, and that doing so would lead a skilled worker to a method meeting the limitations of claim 82.

B. 35 U.S.C. § 112, first paragraph rejections

The Examiner finds that "the specification does not reasonably provide enablement for identifying two or more metalloproteases in a mixed sample using a single signal element wherein the metalloproteases are not initially separated" (Ans. 7). The Examiner also finds that the "specification fails to describe how, if both metalloproteases are in the same physical location and identified with the same label, the artisan would know whether the mixed sample comprised the first metalloprotease, the second metalloprotease, or both metalloproteases" (Ans. 8).

Appellants argue that "the specification, in combination with what is generally known to one of ordinary skill in the art, fully enables claim 90" (App. Br. 19). Appellants argue that "there is no element of claim 90 that is not adequately supported by the written description of the application as filed" (App. Br. 24).

In view of these conflicting positions, we frame the enablement and description issues before us as follows:

(i) Does the evidence of record support the Examiner's conclusion that the specification does not reasonably provide enablement for identifying two or more metalloproteases in a mixed sample using a single signal element wherein the metalloproteases are not initially separated?

(ii) Does the evidence of record support the Examiner's conclusion that the specification fails to provide descriptive support for claim 90?

Findings of Fact

14. The Specification teaches that "[s]ensors of the present invention can comprise a plurality of reaction sites for simultaneous detection of more than one proteinase enzyme" (Spec. 7, ll. 3-4).

15. The Specification teaches that "signal element can be any composition containing any indicator known in the art that provides a detectable and/or measurable manifestation, without a chemical reaction, when the signal element is concentrated in one location" (Spec. 8, ll. 30-33).

16. The Specification teaches that "[s]ignal elements can include, but are not limited to, colorimetric compounds, fluorophores, chemo-illuminescent compounds, magnetic compounds, radioactive compounds, compounds that can be detected potentiometrically, light diffraction elements, or combinations thereof" (Spec. 8, ll. 33-36).

17. In Example 6, the Specification teaches an ELISA assay in which MMPs 1, 8, and 9 were detected (*see, e.g.*, Spec. 17, ll. 27-32 and Fig. 6) The Specification teaches that the "assay was performed the same as in Example 5" (Spec. 17, ll. 29-30).

18. In Example 5, the Specification teaches that the single signal element was the label Pacific Blue, and that "a goat anti-mouse secondary antibody, conjugated to Pacific Blue . . . was utilized for the detection phase of the ELISA assay" (Spec. 17, ll. 13-15).

Principles of Law

> When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application.

In re Wright, 999 F.2d 1557, 1561-62 (Fed. Cir. 1993). "[T]he question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation 'must not be unduly extensive.'" *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

"In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue." *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000). A disclosure provides adequate written description if it conveys with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. *See id.*

Analysis

We again begin with claim interpretation. Claim 90 requires that "the first signal element and the second signal element are the same". We interpret "signal element" consistent with the Specification as "any indicator known in the art that provides a detectable and/or measurable manifestation" (Spec. 8, ll. 30-32; FF 15). Therefore, Claim 90 requires the use of the identical indicator in the detection method.

The Specification not only teaches, but actually exemplifies, a well known and standard assay for simultaneously identifying proteins using a

single signal element which detects two different target antibodies. Specifically, in Example 6, the Specification teaches an ELISA assay in which MMPs 1, 8, and 9 were detected (*see, e.g.*, Spec. 17, ll. 27-32 and Fig. 6) The Specification teaches that the "assay was performed the same as in Example 5" (Spec. 17, ll. 29-30; FF 17). In Example 5, the Specification teaches that the single signal element was the label Pacific Blue, and that "a goat anti-mouse secondary antibody, conjugated to Pacific Blue . . . was utilized for the detection phase of the ELISA assay" (Spec. 17, ll. 13-15; FF 18).

Therefore, the Specification exemplifies detection of multiple MMPs where the first and second signal elements are the same (FF 17-18).

We are not persuaded by the Examiner's argument that the "specification fails to describe how, if both metalloproteases are in the same physical location and identified with the same label, the artisan would know whether the mixed sample comprised the first metalloprotease, the second metalloprotease, or both metalloproteases" (Ans. 8).

This argument misreads Claims 82 and 90 to require that the MMPs are in the same physical location. There is no requirement in either Claim 82 or Claim 90 for the MMP antibodies to be in the same physical location. The requirements in the claims are that the MMPs are simultaneously detected and Claim 90 further requires that the same signal element is used for detection of both target antibodies (*see* Claims 82 and 90). The use of ELISA assays for such detection with the same "signal element" is both remarkably well known and is exemplified in the Specification (FF 17-18).

Conclusions of Law

(i) The evidence of record does not support the Examiner's conclusion that the specification does not reasonably provide enablement for identifying two or more metalloproteases in a mixed sample using a single signal element wherein the metalloproteases are not initially separated.

(ii) The evidence of record does not support the Examiner's conclusion that the specification fails to provide descriptive support for claim 90.

SUMMARY

In summary, we affirm the rejection of claim 82 under 35 U.S.C. § 103(a) as obvious over Sorsa, Rowe, and Sodek. Pursuant to 37 C.F.R. § 41.37(c)(1)(vii)(2006), we also affirm the rejection of claims 83-96 as these claims were not argued separately.

We reverse the rejections of claim 90 under 35 U.S.C. § 112, first paragraph enablement and written description.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

AFFIRMED

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